Application No.	Applicant(s)
09/707 468	NICOLAIDES ET AL
Examiner	**Art Unit**
Dave Nguyen	1633

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-72 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-72 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-4, 9-11, 22-25, 29, readable on a method for the making of a hypermutated antigen comprising administering a polynucleotide comprising a dominant negative allele of a PMS2 mismatched repair gene into an isolated mammalian cell expression a preselected antigen or an *in vivo* cell expressing a preselected antigen of a mammal, readable on class 435, subclasses 325 and 455, class 514, subclass 44.

Should Group I be elected, the group claims will be examined to the extent that the claims are encompassed by the elected group.

II. Claims 1-2, 5, 23, 26, 22, readable on a method for the making of a hypermutated antigen comprising administering a polynucleotide comprising a dominant negative allele of a MLH1 mismatched repair gene into an isolated mammalian cell expression a preselected antigen or an *in vivo* cell expressing a preselected antigen of a mammal, readable on class 435, subclasses 325 and 455, class 514, subclass 44.

Should Group II be elected, the group claims will be examined to the extent that the claims are encompassed by the elected group.

III. Claims 1-2, 6, 23, 27, 22, readable on a method for the making of a hypermutated antigen comprising administering a polynucleotide comprising a dominant negative allele of a PMS1 mismatched repair gene into an isolated mammalian cell expression a preselected antigen or an *in vivo* cell expressing a preselected antigen of a mammal, readable on class 435, subclasses 325 and 455, class 514, subclass 44.

Should Group III be elected, the group claims will be examined to the extent that the claims are encompassed by the elected group.

IV. Claims 1-2, 7-8, 22, readable on a method for the making of a hypermutated antigen comprising administering a polynucleotide comprising a dominant negative allele of a MSH2 mismatched repair gene into an isolated mammalian cell expression a preselected antigen or an *in vivo* cell expressing a preselected antigen of a mammal, readable on class 435, subclasses 325 and 455, class 514, subclass 44.

Should Group IV be elected, the group claims will be examined to the extent that the claims are encompassed by the elected group.

V. Claims 1, 12-15, 19-22, readable on a method for the making a transgenic animal comprising administering a polynucleotide comprising a dominant negative allele of a PMS2 mismatched repair gene into a fertilized egg of a mammal, readable on class 800, subclass 25.

VI. Claims 1, 12-13, 16, 22, readable on a method for the making a transgenic animal comprising administering a polynucleotide comprising a dominant negative allele of a MLH1 mismatched repair gene into a fertilized egg of a mammal, readable on class 800, subclass 25.

VII. Claims 1, 12-13, 17, 22, readable on a method for the making a transgenic animal comprising administering a polynucleotide comprising a dominant negative allele of a PMS1 mismatched repair gene into a fertilized egg of a mammal, readable on class 800, subclass 25.

VIII. Claims 18, 23 and 28, readable on a method for the making of a hypermutated antigen comprising administering a polynucleotide comprising a dominant negative allele of human muTL homolog mismatched repair gene into an isolated mammalian cell expression a preselected antigen or an

in vivo cell expressing a preselected antigen of a mammal, readable on class 435, subclasses 325 and 455, class 514, subclass 44.

Should Group VIII be elected, the group claims will be examined to the extent that the claims are encompassed by the elected group.

IX. Claims 30-32, readable on a nucleic acid assay for determining a mutation in a gene encoding an antigen of interest, classifiable in class 435, subclass 6.

X. Claims 30 and 33, readable on a protein assay for determining a mutation in a gene encoding an antigen of interest, classifiable in class 435, subclass 7.1.

XI. Claims 30 and 34, readable on a phenotypic assay by using a transgenic animal for determining a mutation in a gene encoding an antigen of interest, classifiable in class 800, subclass 3.

XII. Claims 30 and 35, readable on an antibody assay for determining a mutation in a gene encoding an antigen of interest, classifiable in class 435, subclass 7.1.

XIII. Claims 36-41, readable on an *in vitro* method of testing a cell comprising the use of an antisense sequence targeted against an an allele of a mismatch repair gene, whereby said testing embraces assays for determining function(s) and structure(s) of the gene, classifiable in class 435, subclasses 6 and 7.1.

XIV. Claims 36-41, readable on an *in vivo* method of testing a cell comprising the use of an antisense sequence targeted against an an allele of a mismatch repair gene, whereby said testing embraces assays for determining function(s) and structure(s) of the gene, classifiable in class 514, subclass 44.

XV. Claims 42-51, readable on an *in vitro* method of testing a cell comprising a gene encoding a an antigen of interest and a polynucleotide encoding a dominant negative allele of a mismatch repair gene, whereby said testing embraces assays for determining the cell harbors a mutation in said gene that results in at least one new biochemical feature of said antigen, and *in vitro* transgenic cells, classifiable in class 435, subclasses 6 and 7.1.

XVI. Claims 42-56, readable on an *in vivo* method of testing a cell comprising a gene encoding a an antigen of interest and a polynucleotide encoding a dominant negative allele of a mismatch repair gene, whereby said testing embraces assays for determining the cell harbors a mutation in said gene that results in at least one new biochemical feature of said antigen, and *in vivo* transgenic cells obtained from a transgenic mammal, classifiable in class 800, subclasses 3 and 8.

XVII. Claims 57, 60, 64-65, readable on a method of producing a mutated antigen in a reversibly unstable cell, comprising the use of an inducible expression vector comprising a polynucleotide encoding a dominant negative allele of a MLH1 mismatch repair gene, classifiable in class 514, subclass 44.

XVIII. Claims 57, 61, 64-65, readable on a method of producing a mutated antigen in a reversibly unstable cell, comprising the use of an inducible expression vector comprising a polynucleotide encoding a dominant negative allele of a PMS1 mismatch repair gene, classifiable in class 514, subclass 44.

XIX. Claims 57, 62, 65-65, readable on a method of producing a mutated antigen in a reversibly unstable cell, comprising the use of an inducible expression vector comprising a polynucleotide encoding a dominant negative allele of a human *mutL* homolog mismatch repair gene, classifiable in class 514, subclass 44.

XX. Claims 66-68, and 72, readable on a method of producing genetically altered antibodies comprising steps of transfectiing an antibody encoded DNA in to a PMS2 expressing cells and of screening and isolating hypermutated DNA encoding the antibodies, classifiable in class 424, subclass 130.1.

XXI. Claims 66 and 69, readable on a method of producing genetically altered antibodies comprising steps of transfectiing an antibody encoded DNA in to a MLH1 expressing cells and of screening and isolating hypermutated DNA encoding the antibodies, classifiable in class 424, subclass 130.1.

XXII. Claims 66 and 70, readable on a method of producing genetically altered antibodies comprising steps of transfectiing an antibody encoded DNA in to a PMS1 expressing cells and of screening and isolating hypermutated DNA encoding the antibodies, classifiable in class 424, subclass 130.1.

XXIII. Claims 66 and 71, readable on a method of producing genetically altered antibodies comprising steps of transfectiing an antibody encoded DNA in to a human *mutL* homolog expressing cells and of screening and isolating hypermutated DNA encoding the antibodies, classifiable in class 424, subclass 130.1.

XVII. Claims 61-65, readable on a polynucleotide sequence comprising a 3' sequence encoding a plurality of histidine residues, a 5' leader sequence of an expressed gene, and a polylinker, and a method of making a mutated antigen by using the polynucleotide sequence, classifiable in class 435, subclass 320.1, and subclass 325.

XVIII. Claims 66-69, readable on a hypermutated antigen and a method of using the antigen to elicit an immune response in a mammal, classifiable in class 424, subclass 184.1.

Claim 1 links inventions I-VIII. Claim 30 links inventions IX to XII. Claim 36 links inventions XIII and XIV. Claim 42 links invention XV and XVI. Claim 57 links invention XVII to IXX. Claim 66 links inventions XX to XXIII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s). Upon the allowance of the linking claims, the restriction requirement as to the linked invention shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such (claim(s) depending from or including all the limitations of the allowable lining claim(s) is/are presented in a continuation or divisional application, the claims or the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler,* 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The inventions are distinct, each from the other because of the following reasons:

Although there are no provisions under the section for "Relationship of Inventions" in MPEP 806.05 for inventive groups that are directed to <u>different</u> methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct inventions for the following reasons: Methods cited in inventions I-XXIII are directed to different goal(s) and comprise materially distinct steps that render the methods patentably distinct with respect to their functions and their sites of action. For example, the claimed invention of Group I comprises the step of employing a dominant negative allele of a PMS2 mismatch repair gene, whereas the claimed invention of Group II embraces method steps of employing a dominant negative allele of a MLH 1 mismatch repair gene.

Given that an enormous number of distinct inventions are claimed in the pending claims and comprise materially distinct steps and/or generate different functions and effects, as indicated in preceding paragraphs, and thus, are not required for use together, it would also be unduly burdensome for the examiner to search and/or consider the patentability of the claims that embrace distinct inventions.

Because the inventions are distinct for the reasons given above and have acquired a separate status in the art because of their divergent subject matter, fall into different statutory classes of invention, and are separately classified and searched, restriction for examination purposes as indicated is proper..

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst Kimberly Davis, whose telephone number is **(703) 305-3015**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(703) 305-2024**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Deborah Clark*, may be reached at **(703) 305-4051.**

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Nguyen
Patent Examiner
Art Unit: 1633

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PRIMARY EXAMINER

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